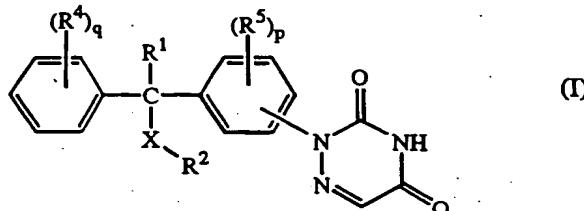


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Claims

1. A compound of formula



a *N*-oxide, a pharmaceutically acceptable addition salt or a stereochemically isomeric

5 form thereof, wherein :

p represents an integer being 0, 1, 2, 3 or 4;

q represents an integer being 0, 1, 2, 3, 4 or 5;

X represents O, S, NR³ or a direct bond;

10 R¹ represents hydrogen, hydroxy, halo, amino, mono- or di(C₁-4alkyl)amino, C₁-6alkyl, C₁-6alkyloxy, C₃-7cycloalkyl, aryl, arylC₁-6alkyl, aminoC₁-4alkyl, mono- or di(C₁-4alkyl)aminoC₁-4alkyl or mono- or di(C₁-4alkyl)aminoC₁-4alkylamino;

15 R² represents aryl, Het¹, C₃-7cycloalkyl, C₁-6alkyl or C₁-6alkyl substituted with one or two substituents selected from hydroxy, cyano, amino, mono- or di(C₁-4alkyl)amino, C₁-6alkyloxy, C₁-6alkylsulfonyloxy, C₁-6alkyloxycarbonyl, C₃-7cycloalkyl, aryl, aryloxy, arylthio, Het¹, Het¹oxy and Het¹thio; and if X is O, S or NR³, then R² may also represent aminocarbonyl, aminothiocarbonyl, C₁-4alkylcarbonyl, C₁-4alkylthiocarbonyl, arylcarbonyl or arylthiocarbonyl;

R³ represents hydrogen or C₁-4alkyl;

each R⁴ independently represents C₁-6alkyl, halo, polyhaloC₁-6alkyl, hydroxy, mercapto, C₁-6alkyloxy, C₁-6alkylthio, C₁-6alkylcarbonyloxy, aryl, cyano, nitro, Het³, R⁶, NR⁷R⁸ or C₁-4alkyl substituted with Het³, R⁶ or NR⁷R⁸;

20 each R⁵ independently represents C₁-6alkyl, halo, polyhaloC₁-6alkyl, hydroxy, mercapto, C₁-6alkyloxy, C₁-6alkylthio, C₁-6alkylcarbonyloxy, aryl, cyano, nitro, Het³, R⁶, NR⁷R⁸ or C₁-4alkyl substituted with Het³, R⁶ or NR⁷R⁸;

25 each R⁶ independently represents C₁-6alkylsulfonyl, aminosulfonyl, mono- or di(C₁-4alkyl)aminosulfonyl, mono- or di(benzyl)aminosulfonyl, polyhaloC₁-6alkylsulfonyl, C₁-6alkylsulfinyl, phenylC₁-4alkylsulfonyl, piperazinylsulfonyl, aminopiperidinylsulfonyl, piperidinylaminosulfonyl, N-C₁-4alkyl-N-piperidinylaminosulfonyl;

30 each R⁷ and each R⁸ are independently selected from hydrogen, C₁-4alkyl, hydroxyC₁-4alkyl, dihydroxyC₁-4alkyl, aryl, arylC₁-4alkyl, C₁-4alkyloxyC₁-4alkyl, C₁-4alkylcarbonyl, arylcarbonyl, C₁-4alkylcarbonyloxyC₁-4alkylcarbonyl, hydroxyC₁-4alkylcarbonyl, C₁-4alkyloxycarbonylcarbonyl, mono- or

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- di(C₁₋₄alkyl)aminoC₁₋₄alkyl, arylaminocarbonyl, arylaminothiocarbonyl,
Het³aminocarbonyl, Het³aminothiocarbonyl, C₃₋₇cycloalkyl, pyridinylC₁₋₄alkyl, Het³ and R⁶;
- R⁹ and R¹⁰ are each independently selected from hydrogen, C₁₋₄alkyl, hydroxyC₁₋₄alkyl,
5 dihydroxyC₁₋₄alkyl, phenyl, phenylC₁₋₄alkyl, C₁₋₄alkyloxyC₁₋₄alkyl, C₁₋₄alkylcarbonyl,
phenylcarbonyl, C₁₋₄alkylcarbonyloxyC₁₋₄alkylcarbonyl, hydroxyC₁₋₄alkylcarbonyl,
C₁₋₄alkyloxycarbonylcarbonyl, mono- or di(C₁₋₄alkyl)aminoC₁₋₄alkyl,
phenylaminocarbonyl, phenylaminothiocarbonyl, Het³aminocarbonyl,
10 Het³aminothiocarbonyl, C₃₋₇cycloalkyl, pyridinylC₁₋₄alkyl, Het³ and R⁶;
- each R¹¹ independently being selected from hydroxy, mercapto, cyano, nitro, halo,
trihalomethyl, C₁₋₄alkyloxy, carboxyl, C₁₋₄alkyloxycarbonyl,
15 trihaloC₁₋₄alkylsulfonyloxy, R⁶, NR⁷R⁸, C(=O)NR⁷R⁸, aryl, aryloxy, arylcarbonyl,
C₃₋₇cycloalkyl, C₃₋₇cycloalkyloxy, phthalimide-2-yl, Het³ and C(=O)Het³;
- R¹² and R¹³ are each independently selected from hydrogen, C₁₋₄alkyl, hydroxyC₁₋₄alkyl,
15 dihydroxyC₁₋₄alkyl, phenyl, phenylC₁₋₄alkyl, C₁₋₄alkyloxyC₁₋₄alkyl, C₁₋₄alkylcarbonyl,
phenylcarbonyl, C₁₋₄alkylcarbonyloxyC₁₋₄alkylcarbonyl, hydroxyC₁₋₄alkylcarbonyl,
C₁₋₄alkyloxycarbonylcarbonyl, mono- or di(C₁₋₄alkyl)aminoC₁₋₄alkyl,
phenylaminocarbonyl, phenylaminothiocarbonyl, C₃₋₇cycloalkyl, pyridinylC₁₋₄alkyl and
R⁶;
- 20 aryl represents phenyl optionally substituted with one, two or three substituents each
independently selected from nitro, azido, halo, hydroxy, C₁₋₄alkyl, C₁₋₄alkyloxy,
polyhaloC₁₋₄alkyl, NR⁹R¹⁰, R⁶, phenyl, Het³ and C₁₋₄alkyl substituted with NR⁹R¹⁰;
- Het¹ represents a heterocycle selected from pyrrolyl, pyrrolinyl, imidazolyl, imidazolinyl,
pyrazolyl, pyrazolinyl, triazolyl, tetrazolyl, furanyl, tetrahydrofuranyl, thienyl, thiolanyl,
25 dioxolanyl, oxazolyl, oxazolinyl, isoxazolyl, thiazolyl, thiazolinyl, isothiazolyl,
thiadiazolyl, oxadiazolyl, pyridinyl, pyrimidinyl, pyrazinyl, pyranyl, pyridazinyl,
pyrrolidinyl, piperidinyl, piperazinyl, morpholinyl, thiomorpholinyl, dioxanyl, dithianyl,
trithianyl, triazinyl, benzothienyl, isobenzothienyl, benzofuranyl, isobenzofuranyl,
benzothiazolyl, benzoxazolyl, indolyl, isoindolyl, indolinyl, purinyl, 1H-pyrazolo[3,4-d]pyrimidinyl, benzimidazolyl, quinolyl, isoquinolyl, cinnolinyl, phtalazinyl,
30 quinazolinyl, quinoxalinyl, thiazolopyridinyl, oxazolopyridinyl, imidazo[2,1-b]thiazolyl;
wherein said heterocycles each independently may optionally be substituted with one,
or where possible, two or three substituents each independently selected from Het², R¹¹
and C₁₋₄alkyl optionally substituted with Het² or R¹¹;
- 35 Het² represents a monocyclic heterocycle selected from pyrrolyl, pyrrolinyl, imidazolyl,
imidazolinyl, pyrazolyl, pyrazolinyl, triazolyl, tetrazolyl, furanyl, tetrahydrofuranyl,
thienyl, thiolanyl, dioxolanyl, oxazolyl, oxazolinyl, isoxazolyl, thiazolyl, thiazolinyl,

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isothiazolyl, thiadiazolyl, oxadiazolyl, pyridinyl, pyrimidinyl, pyrazinyl, pyranyl, pyridazinyl, dioxanyl, dithianyl, trithianyl and triazinyl; wherein said monocyclic heterocycles each independently may optionally be substituted with one, or where possible, two or three substituents each independently selected from R¹¹ and C₁₋₄alkyl optionally substituted with R¹¹;

Het³ represents a monocyclic heterocycle selected from pyrrolidinyl, piperidinyl, piperazinyl, morpholinyl, thiomorpholinyl; wherein said monocyclic heterocycles each independently may optionally be substituted with, where possible, one, two or three substituents each independently selected from C₁₋₄alkyl, C₁₋₄alkyloxy, carboxyl, C₁₋₄alkyloxycarbonyl, C₁₋₄alkylcarbonyl, phenylC₁₋₄alkyl, piperidinyl, NR¹²R¹³, R⁶ and C₁₋₄alkyl substituted with R⁶ or NR¹²R¹³.

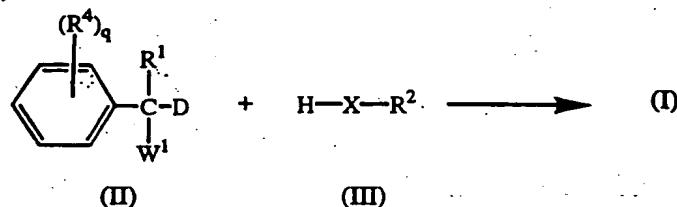
2. A compound according to claim 1 wherein R¹ is hydrogen, hydroxy, halo, amino, C₁₋₆alkyl, C₁₋₆alkyloxy or mono- or di(C₁₋₄alkyl)aminoC₁₋₄alkylamino.
- 15 3. A compound according to claim 1 or 2 wherein R² is aryl, Het¹, C₃₋₇cycloalkyl, or C₁₋₆alkyl substituted with one or two substituents selected from hydroxy, cyano, amino, mono- or di(C₁₋₄alkyl)amino, C₁₋₆alkyloxy, C₁₋₆alkylsulfonyloxy, C₁₋₆alkyloxycarbonyl, C₃₋₇cycloalkyl, aryl, aryloxy, arylthio, Het¹, Het¹oxy and Het¹thio; and if X is O, S or NR³, then R² may also represent aminocarbonyl, aminothiocarbonyl, C₁₋₄alkylcarbonyl, C₁₋₄alkylthiocarbonyl, arylcarbonyl or arylthiocarbonyl.
- 20 4. A compound according to any one of claims 1 to 3 wherein the 6-azauracil moiety is in the para position relative to the central carbon atom.
- 25 5. A compound according to any one of claims 1 to 4 wherein q is 1 or 2 and one R⁴ substituent is in the 4 position; and p is 1 or 2 and the one or two R⁵ substituents are in the ortho position relative to the central carbon atom.
- 30 6. A composition comprising a pharmaceutically acceptable carrier and, as active ingredient, a therapeutically effective amount of a compound as claimed in any one of claims 1 to 5.
- 35 7. A process for preparing a composition as claimed in claim 6, , wherein a pharmaceutically acceptable carrier is intimately mixed with a therapeutically effective amount of a compound as defined in any one of claims 1 to 5.
8. A compound as claimed in any one of claims 1 to 5 for use as a medicine.

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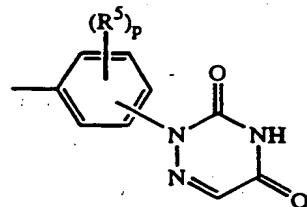
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9. Use of a compound as claimed in any one of claims 1 to 5 in the manufacture of a medicament for treating eosinophil-dependent inflammatory diseases.

5 10. A process for preparing a compound as claimed in claim 1, characterized by,
a) reacting an intermediate of formula (II) wherein W¹ is a suitable leaving group with an appropriate reagent of formula (III) optionally in a reaction-inert solvent and in the presence of a base;

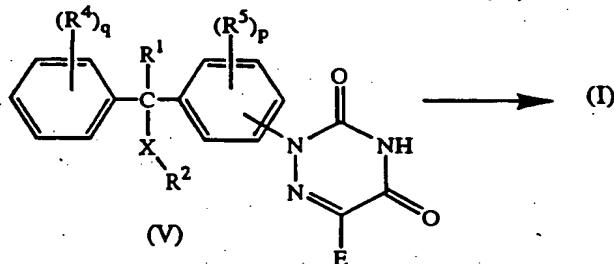


- 10 wherein R^1 , R^2 , R^4 , X and q are as defined in claim 1, and D represents

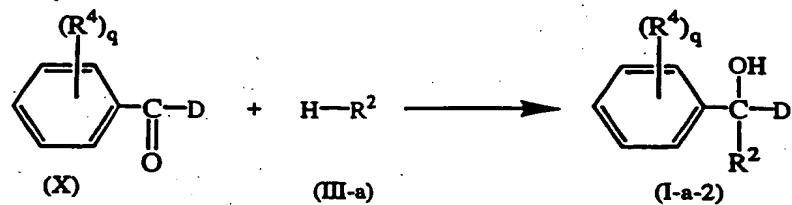


wherein R⁵ and p are defined as in claim 1;

b) eliminating the group E of a triazinedione of formula (V)



- 15 wherein R¹, R², R⁴, R⁵, X and q are as defined in claim 1;
c) reacting a ketone of formula (X) with an intermediate of formula (III-a) in the presence of a base and in a reaction-inert solvent; thus obtaining a compound of formula (I-a-2);

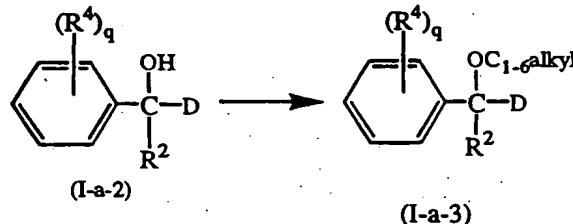


- 20 wherein R^2 , R^4 and q are as defined in claim 1 and D is defined as in claim 9a);

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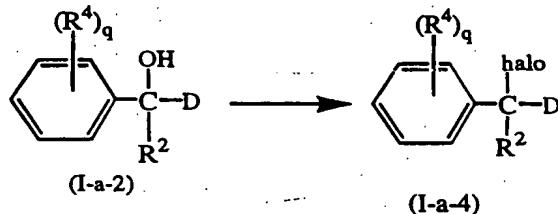
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d) converting a compound of formula (I-a-2) to a compound of formula (I-a-3) using art-known group transformation reactions,



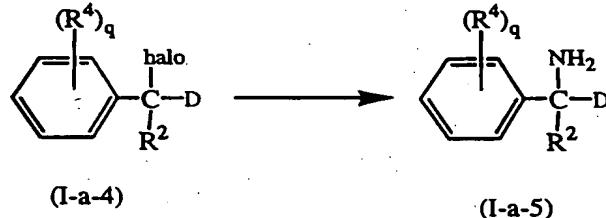
wherein R^2 , R^4 and q are as defined in claim 1 and D is defined as in claim 9a);

5 e) converting a compound of formula (I-a-2) to a compound of formula (I-a-4) using art-known group transformation reactions,



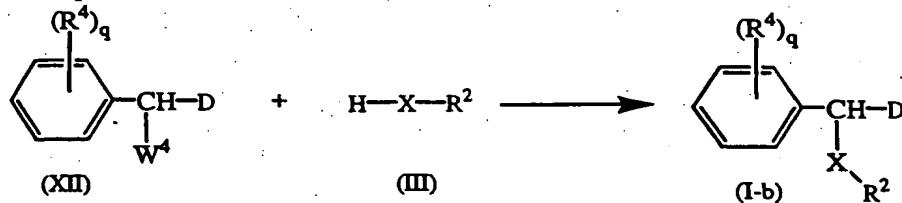
wherein R^2 , R^4 and q are as defined in claim 1 and D is defined as in claim 9a);

f) converting a compound of formula (I-a-4) to a compound of formula (I-a-5) using
10 art-known group transformation reactions,



wherein R^2 , R^4 and q are as defined in claim 1 and D is defined as in claim 9a);

15 g) reacting an intermediate of formula (XII) wherein W^4 is a suitable leaving group with an intermediate of formula (III) optionally in the presence of a suitable base; thus obtaining a compounds of formula (I-b);



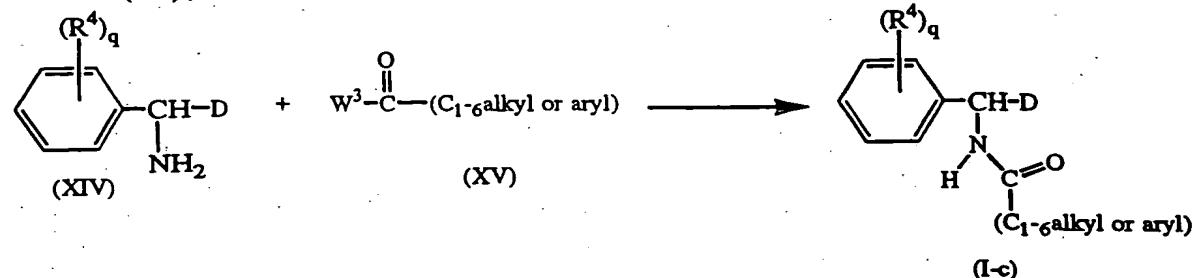
wherein R^2 , R^4 , X and q are as defined in claim 1 and D is defined as in claim 9a);

h) reacting an intermediate of formula (XIV) with an intermediate of formula (XV) wherein W^3 is a suitable leaving group, in the presence of a suitable base and

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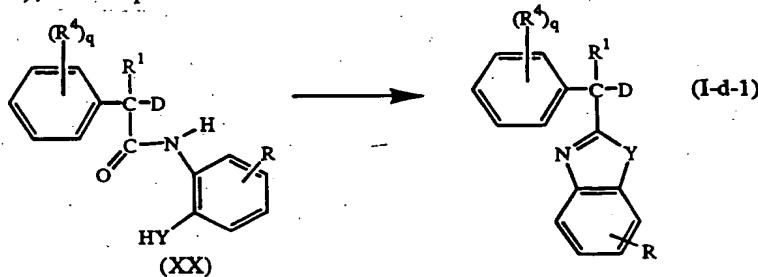
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optionally in the presence of a reaction-inert solvent; thus obtaining a compound of formula (I-c);



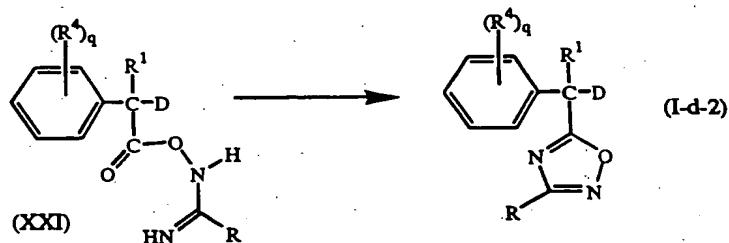
wherein R^4 and q are as defined in claim 1 and D is defined as in claim 9a);

- 5 i) cyclizing an intermediate of formula (XX) wherein Y is O, S or NR^3 , to a compound of formula (I-d-1), in the presence of a suitable solvent at an elevated temperature;



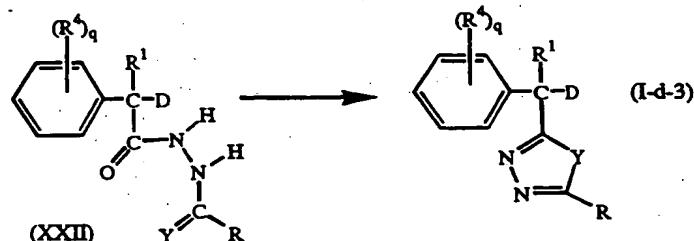
wherein R, R^1 , R^4 and q are as defined in claim 1 and D is defined as in claim 9a);

- 10 j) cyclizing an intermediate of formula (XXI) to a compound of formula (I-d-2) in a reaction-inert solvent at an elevated temperature,



wherein R, R^1 , R^4 and q are as defined in claim 1 and D is defined as in claim 9a);

- k) cyclizing an intermediate of formula (XXII) wherein Y is O, S or NR^3 , to a compound of formula (I-d-3), in a suitable solvent,



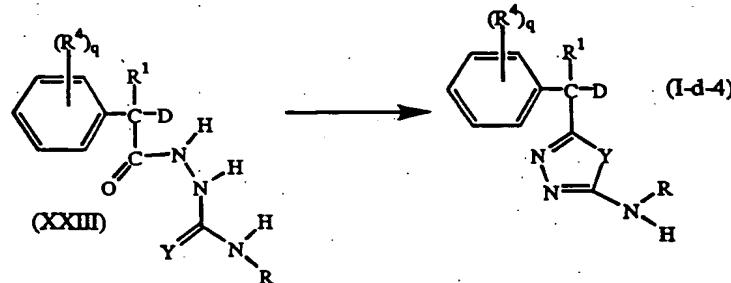
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wherein R, R^1 , R^4 and q are as defined in claim 1 and D is defined as in claim 9a);

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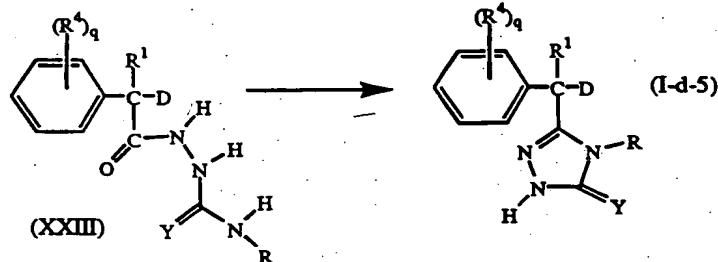
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- 1) cyclizing an intermediate of formula (XXIII) wherein Y is O, S or NR³, to a compound of formula (I-d-4), in a reaction-inert solvent and in the presence of an acid,



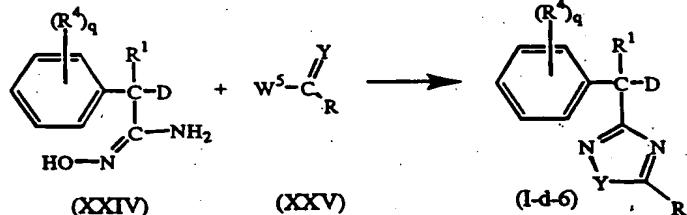
wherein R, R¹, R⁴ and q are as defined in claim 1 and D is defined as in claim 9a);

- 5 m) cyclizing an intermediate of formula (XXIII) wherein Y is O, S or NR³, to a compound of formula (I-d-5), in a reaction-inert solvent and in the presence of an acid,



wherein R, R¹, R⁴ and q are as defined in claim 1 and D is defined as in claim 9a);

- n) reacting an intermediate of formula (XXIV) with an intermediate of formula (XXV) wherein Y is O, S or NR³, and W⁵ is a suitable leaving group; thus forming a compound of formula (I-d-6) in a reaction-inert solvent and in the presence of a base,

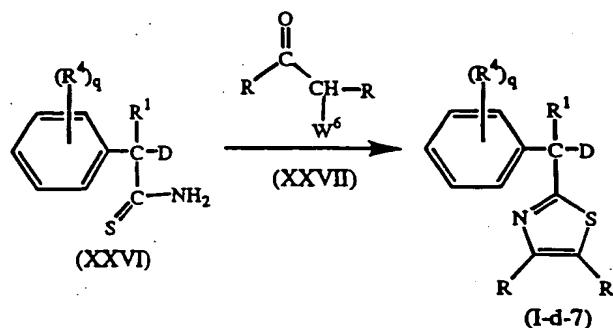


wherein R, R¹, R⁴ and q are as defined in claim 1 and D is defined as in claim 9a);

- o) reacting an intermediate of formula (XXVI) with an intermediate of formula (XXVII) wherein W⁶ is a suitable leaving group; thus forming a compound of formula (I-d-7), in a reaction-inert solvent and in the presence of an acid;

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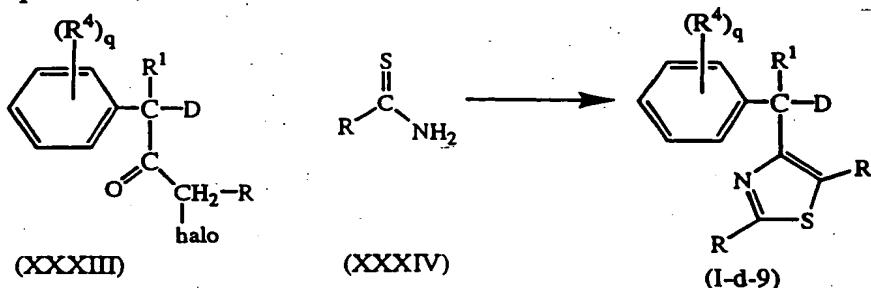
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wherein R, R¹, R⁴ and q are as defined in claim 1 and D is defined as in claim 9a);

p) reacting an intermediate of formula (XXXIII) with a thioamide of formula (XXXIV); thus forming a compound of formula (I-d-9) in a reaction-inert solvent at an elevated temperature;

5



wherein R, R¹, R⁴ and q are as defined in claim 1 and D is defined as in claim 9a);

and if desired, converting compounds of formula (I) into each other following art-known transformations, and further, if desired, converting the compounds of formula (I), into a therapeutically active non-toxic acid addition salt by treatment with an acid, or into a therapeutically active non-toxic base addition salt by treatment with a base, or conversely, converting the acid addition salt form into the free base by treatment with alkali, or converting the base addition salt into the free acid by treatment with acid; and also, if desired, preparing stereochemically isomeric forms or N-oxide forms thereof.

15

11. A process of marking a receptor comprising the steps of
 - a) radiolabelling a compound as defined in claim 1;
 - b) administering said radiolabelled compound to biological material,
 - c) detecting the emissions from the radiolabelled compound.

20

12. A process of imaging an organ, characterized by, administering a sufficient amount of a radiolabelled compound of formula (I) in an appropriate composition, and detecting the emissions from the radioactive compound.